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10/578,937	10/12/2006	Per Olaf Ekstrom	3637.1000-003	2233

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EXAMINER	
KASTEN, ROBERT J	

ART UNIT	PAPER NUMBER
1795	

MAIL DATE	DELIVERY MODE
08/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,937	EKSTROM, PER OLAF	
	Examiner	Art Unit	
	ROBERT KASTEN	1795	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/15/2008, 10/09/2007, 07/16/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is the first non-final action on the merits.

Claims 1-22 are pending in this application.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1-5, 8-15 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by MINARIKOVA (US 2004/0118685), from here on referred to as MINARIKOVA.

Concerning Claim 1, MINARIKOVA teaches a method for electrophoretic separation (title) of nucleic acids (DNA, [0003]), comprising the steps of injecting a sample into a capillary, separating the sample in the capillary by electrophoresis [0017], where the temperature of the system is cycled [0019] at least two times [0022] between a high and a low temperature [0020]. Because the electrophoresis is considered "classical capillary electrophoretic separation [0017]," the method would inherently have the sample applied to a gel matrix in the electrophoresis capillary.

Concerning Claim 2, MINARIKOVA teaches using the method to detect DNA polymorphisms [0007 and 0009]. Therefore, MINARIKOVA teaches that the nucleic acids of claim 1 can be polymorphic DNA sites.

Concerning Claim 3, MINARIKOVA inherently teaches that allelic variants at the one or more polymorphic sites are separated. Since alleles are simply alternative, or in some cases mutated, DNA sequences, and all DNA is inherently made up of nucleic acids, the ability for the prior art method to separate DNA and distinguish between different DNA mutations and polymorphisms [0009] would lead one of ordinary skill in the art to the conclusion that this method is inherently capable of separating allelic variants as well.

Concerning Claim 4, MINARIKOVA teaches that the temperature of the system is cycled from a high temperature to a lower temperature [0021].

Concerning Claim 5, MINARIKOVA teaches a claim 12 which states that the cycling temperature gradient can have variable temperature range cycles. Variable temperature range cycles read on different temperatures on successive cycles.

Concerning Claim 8, MINARIKOVA teaches that the temperature be cycled between a high temperature about 3 degrees higher than the low temperature (52 °C - 50 °C) [0021].

Concerning Claim 9, MINARIKOVA teaches that the temperature be cycled between a high temperature 2 degrees higher than the low temperature (52 °C - 50 °C) [0021].

Concerning Claim 10, MINARIKOVA teaches that the temperature be cycled between a high temperature 9 degrees higher than the low temperature (54 °C - 46 °C) [0021].

Concerning Claim 11, MINARIKOVA teaches that the high temperature is less than 80 °C (54 °C) [0020].

Concerning Claim 12, MINARIKOVA teaches that the low temperature can be about 40 °C (46 °C) [0020].

Concerning Claim 13, MINARIKOVA teaches that the high temperature can be 54 °C [0020].

Concerning Claim 14, MINARIKOVA teaches that the low temperature can be 46 °C [0021].

Concerning Claim 15, MINARIKOVA teaches that the samples (dsDNA, [0009]) is continuously detected [0022].

Concerning Claim 21, MINARIKOVA teaches a method for electrophoretic separation (title) of nucleic acids (DNA, [0003]), comprising the steps of injecting a sample into a capillary, separating the sample in the capillary by electrophoresis, where the temperature of the system is cycled [0019] at least two times [0022] between a high and a low temperature [0020]. Finally, the method of MINARIKOVA is inherently capable of detecting a microhaplotype. Since haplotypes are simply combinations of alleles, and alleles simple variations or mutations on the nucleic acid sequences in DNA, the ability for the prior art method to separate DNA and distinguish between different DNA mutations and polymorphisms [0009] would lead one of ordinary skill in

the art to the conclusion that this method is inherently capable of separating microhaplotypes as well.

3. Claims 18-19 are rejected under 35 U.S.C. 102(a) as being anticipated by BJORHEIM et al. (*J. Sep. Sci.* 2003, *26*, 1163-1168).

Concerning Claim 18, BJORHEIM teaches a method for evaluating denaturing conditions of DNA variants in multi-capillary electrophoresis devices (title), comprising the following steps:

- Carrying out electrophoresis in a 96-capillary matrix (pg. 1164, 2.3 CE). The capillaries contain linear polyacrylamide, inherently creating a capillary gel electrophoresis matrix to sample separation.
- Cycling the temperature at various time intervals (pg. 1164, 2.4 "Denaturing...")
- The temperatures were varied multiple times and were varied from low to high (pg. 1168, col. 1, para. 3)
- The variant sequences were then quantified (pg. 1167, col. 1, para. 2)

BJORHEIM also teaches that quantification of variant sequences can be performed using the peaks in electropherograms (pg. 1168, col. 1, para. 3).

Concerning Claim 19, BJORHEIM teaches that the method further comprises the step of detecting the samples after electrophoresis (laser-induced fluorescence, pg. 1164, 2.3 CE).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over MINARIKOVA in view of BJORHEIM.

Concerning Claims 6-7, MINARIKOVA teaches all the limitations of claim 1. Further, MINARIKOVA teaches that the number of temperature cycles can be optimized to provide increased sample throughput because it enables the use of a multiple-injection technique for sample loading [0019].

MINARIKOVA does not teach a specific number of temperature cycles.

However, BJORHEIM teaches that the number of temperature cycles can be about 20 (15 from pg. 1166, col. 2, para. 1).

Temperature cycling (the number, frequency, amplitudes, etc) is considered by the Examiner to be a known result effective variable. In the present case, the prior art reference of MINARIKOVA teaches that the temperature cycles could be used in conjunction with a sample injection technique to facilitate higher sample throughput. Implicitly, it is taught that the amount of temperature cycles can be then scaled to the size of the sample, such that the whole sample, though not necessarily all present in the capillary at the same time, will encounter the same temperature conditions at all times. Because the prior art already teaches that temperature cycles can occur as many as 15 times without adverse effects to the sample (BJORHEIM), there is a reasonable expectation that control of this variable (the number of cycles) in the method of MINARIKOVA would yield expected results. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The discovery of an optimum value of a known result effective variable, without producing any new or unexpected results, is within the ambit of a

person of ordinary skill in the art. See *In re Boesch*, 205 USPQ 215 (CCPA 1980) (see MPEP § 2144.05, II.). Therefore, at the time of the invention, it would have been *prima facie* obvious to those of ordinary skill in the art to operate the method of MINARIKOVA for the duration of BJORHEIM because the number of temperature cycles is a result effective variable that can be optimized to provide high sample throughput and therefore more efficient sample processing.

8. Claims 16-17 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over MINARIKOVA.

Concerning Claim 16, MINARIKOVA does not expressly teach that the DNA sample remain double stranded at the end of the last temperature cycle.

However, MINARIKOVA does teach that the temperatures cycle from high to low and would necessarily end at the lowest temperature of the cycle [0020-0021].

In the present case, especially since the lowest temperature in the range is used as the final temperature of the capillary, the temperature may already be below the melting temperature (Tm) of the DNA. This Tm, however, is dependent on the specific composition of the DNA, and would vary depending on how the user decided to optimize the prior art method. The Tm of a given DNA complex is likely to be known or at least approximated, and behaviors of the complex around the Tm (namely that below the Tm the complex is double-stranded and above the Tm the complex is single-stranded) are the basis for this entire inventive concept. One of ordinary skill in the art would have known that the low temperature on the temperature oscillation sequence

could easily be below the Tm or above the Tm, depending on how the user wished to optimize the method of claim 13. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The discovery of an optimum value of a known result effective variable, without producing any new or unexpected results, is within the ambit of a person of ordinary skill in the art. See *In re Boesch*, 205 USPQ 215 (CCPA 1980) (see MPEP § 2144.05, II.). Therefore, it would have been *prima facie* obvious to those of ordinary skill in the art to set the final temperature of the DNA at the below the Tm of the DNA because the temperature of the system has been shown to be a result-effective variable and optimization of this temperature would have been a matter of design choice.

Concerning Claims 17 and 22, MINARIKOVA does not expressly teach optimization off the temperature ramping to provide optimal separation of alleles.

In the present case, the oscillation of temperature is already taught in the prior art reference of MINARIKOVA. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The discovery of an optimum value of a known result effective variable, without producing any new or unexpected results, is within the ambit of a person of ordinary skill in the art. See *In re Boesch*, 205 USPQ 215 (CCPA 1980) (see MPEP § 2144.05, II.). It would have been obvious to one of ordinary skill in the art to optimize any process, such as the oscillation of temperature, taught in the prior art for improved efficiency of

the process as well as to improve the chances of successfully separating each target species in a sample.

9. Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over BJORHEIM in view of MINARIKOVA.

Concerning Claim 20, BJORHEIM does not expressly teach that the DNA sample remain double stranded at the end of the last temperature cycle.

However, MINARIKOVA does teach that the temperatures cycle from high to low and would necessarily end at the lowest temperature of the cycle [0020-0021].

Temperature cycling (the number, frequency, amplitudes, etc) is considered by the Examiner to be a known result effective variable. In the present case, especially since the lowest temperature in the range is used as the final temperature of the capillary, the temperature may already be below the melting temperature (Tm) of the DNA. This Tm, however, is dependent on the specific composition of the DNA, and would vary depending on how the user decided to optimize the prior art method. The Tm of a given DNA complex is likely to be known or at least approximated, and behaviors of the complex around the Tm (namely that below the Tm the complex is double-stranded and above the Tm the complex is single-stranded) are the basis for this entire inventive concept. One of ordinary skill in the art would have known that the low temperature on the temperature oscillation sequence could easily be below the Tm or above the Tm, depending on how the user wished to optimize the method of claim 13. "[W]here the general conditions of a claim are disclosed in the prior art, it is not

inventive to discover the optimum or workable ranges by routine experimentation." See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The discovery of an optimum value of a known result effective variable, without producing any new or unexpected results, is within the ambit of a person of ordinary skill in the art. See *In re Boesch*, 205 USPQ 215 (CCPA 1980) (see MPEP § 2144.05, II.). Therefore, it would have been *prima facie* obvious to those of ordinary skill in the art to set the final temperature of the DNA at the below the Tm of the DNA because the temperature of the system has been shown to be a result-effective variable and optimization of this temperature would have been a matter of design choice.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT KASTEN whose telephone number is (571)270-7598. The examiner can normally be reached on Mon-Thurs, 8am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Sines can be reached on 571-272-1263. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/R. K./
Examiner, Art Unit 1795

/Brian J. Sines/

Supervisory Patent Examiner, Art Unit 1795